Lung cancer risk in workers exposed to poly(vinyl chloride) dust: a nested case-referent study

G Mastrangelo, U Fedeli, E Fadda, G Milan, A Turato, S Pavanello

Original Article

Background: There have been few investigations of an association between poly(vinyl chloride) (PVC) dust exposure and an increase in lung cancer incidence, and their conclusions have been inconsistent. Aims: To determine whether PVC and/or vinyl chloride monomer (VCM) is the associated risk factor(s), by means of a nested case-referent study, in order to estimate lung cancer risk, avoiding selection, information, or confounding biases.

Methods: Thirty-eight cases of histologically verified lung cancer and 224 control subjects without a history of cancer were selected from an Italian cohort of 1658 vinyl chloride workers. Information sources included clinical records (diagnosis, smoking habits) and plant records (occupational history). The risk of lung cancer was estimated by odds ratios (OR) with 95% confidence intervals (CI), calculated using logistic regression models.

Results: In PVC baggers exposed to high levels of respirable PVC particles in the workplace, the lung cancer OR increases by 20% for each extra year of work (OR = 1.2003; 95% CI 1.0772 to 1.3469; p = 0.0010), when the influence of age and smoking habits is controlled. No relation was found between lung cancer and cumulative PVC exposure.

Conclusion: This nested case-control study showed, in the VCM/PVC industry, an increased risk of lung cancer associated with exposure to PVC dust; previous cohort studies failed to recognise such excess, probably because they used VCM exposure as the risk indicator.

Poly(vinyl chloride) (PVC), one of the most widely used plastic materials, is produced by polymerisation of vinyl chloride monomer (VCM). The VCM/PVC industry was the focus of a major occupational health crisis in the mid-1970s when an increased frequency of the rare liver angiosarcoma tumour was reported in workers exposed to over 10 000 ppm VCM in cleaning reactor vessels. Thereafter, a number of cohort studies were carried out. As some tumours caused by VCM are rare in men, in order to increase the number of cases and the precision of risk estimates, authors extended the follow-up of a given cohort and/or included different cohorts in a larger one, subsequently issuing new reports. Lastly, two megacohorts were assembled, one in the USA and the other in Europe. In a historical quantitative review of all cohort studies linking VCM exposure to cancer, a reduction in cancer risk across calendar time was found for liver (p < 0.00001), brain (p < 0.029), and lung (p < 0.042) tumours in VCM workers, in parallel with the reduction in VCM exposure by three orders of magnitude.

According to Mundt and colleagues, the need for additional follow-up of these cohorts does not appear to be great, except perhaps to verify that the observed excesses continue to decline. Furthermore, cohort studies are unavoidably affected by systematic errors; selection (healthy worker effect), information (misclassification of exposure and diagnosis of diseases based on death certificate), and confounding (smoking) biases. It has been suggested that further studies should use the nested case-control approach.

Lung cancer standardised mortality ratios (SMRs) are generally close to unity in the cohort studies, possibly due to a dilution effect caused by poor characterisation of the relevant exposure. In the early case-referent study nested in a cohort of 4806 workers of four USA plants of PVC polymerisation, an index of cumulative exposure to 12 substances, including VCM and PVC, was estimated in cases and controls. Only the difference in cumulative exposure to PVC was significant (p < 0.037) when the cases of adenocarcinoma and undifferentiated large cell carcinoma were compared with the control series. When updating this cohort, however, Wu et al found no significant relation between the cumulative exposure to PVC (or to VCM) and lung cancer risk in his nested case-referent study. Furthermore, cancer incidence data and person-year mass from 454 workers of a Norwegian polymerisation PVC plant have been used to estimate the lung cancer rate in PVC baggers and dryers (172.2×10̇) as well as in other workers (28.8×10̇), obtaining in the former a risk 5.98 times higher than in the latter. Lastly, the lung cancer risk was lower than unity in baggers-driers from the English cohort of 5498 vinyl chloride workers, even though, among baggers-driers whose first exposure was more than 20 years previously, the observed cases of lung cancer exceeded the expected number.

These few and conflicting results have led to the present study, which considers an Italian cohort where production was divided into three segments: (1) VCM production, occurring in enclosed systems with limited exposures; (2) PVC resin production, where the VCM exposure was highest in the past, particularly during the cleaning of reactor vessels; PVC dust bags is also a characteristic of this segment of the plant; and (3) PVC compounding, involving the addition of plasticisers and other additives to polymerised resin to alter its physical properties. Among the 1658 workers employed in the plant, Pirastu et al reported 10 lung cancer cases in PVC baggers as opposed to the 7.0 expected, an SMR equal to 1.43, with 90% confidence interval (CI) 0.78 to 2.42. In order to estimate lung cancer risk not affected by selection, information, and confounding biases, as well as aiming to find out whether VCM and/or PVC were the associated risk factor(s) if at all, we carried out a case-referent study nested in that cohort.

Abbreviations: CI, confidence interval; OR, odds ratio; PVC, poly(vinyl chloride); SMR, standardised mortality ratio; TLV, threshold limit value; VCM, vinyl chloride monomer
SUBJECTS AND METHODS

The above cohort study was carried out in the event of a lawsuit by hundreds of workers, local municipalities, and the Italian national government against the management of the plant. At the beginning of the lawsuit, the company indemnified any health problem that claimant workers themselves attributed to their past exposure in the plant. Among the 543 “claimants”, we chose 38 cases of histologically verified lung cancer and 224 control subjects without history of cancer and all other claimant workers. The histological types (number of subjects) of the lung cancer were: adenocarcinoma (n = 11); squamous cell carcinoma (n = 15); mixed adenocarcinoma and squamous cell carcinoma (n = 1); bronchoalveolar carcinoma (n = 1); small cell carcinoma (n = 4); and large cell carcinoma (n = 6). In the court documents, we found the diseases (number of subjects) alleged by the controls: liver cirrhosis (n = 8); chronic bronchitis (n = 32); PVC pneumoniosis (n = 8); Raynaud’s syndrome (n = 53); acroosteolysis (n = 6); Dupuytren’s disease (n = 2); blood diseases (n = 1); various associations of the above (n = 16); and changes in liver function, alone (n = 98) or associated with one disease or more.

Information as to job performed and the relative corresponding entry/exit dates was drawn out from the files of the company and the Italian National Social Security Administration by members of the Police Force, who were blind with respect to the case/control status. A table was prepared for each worker. This table, revised due to inconsistencies which emerged during the course of the lawsuit, is the source for the assessment of the occupational exposure.

With regard to job performed, we coded a polytomous variable: 0 (subjects with the least exposure to PVC dust); 1 (compounding workers, never baggers); 2 (PVC baggers with unknown length of job; in these workers, who probably held several jobs at once, the date of the specific job change was not indicated); and 3 (PVC baggers with known length of job, for whom beginning and ending dates were available).

We calculated the job duration in compounding workers and baggers; the median length was used to split the whole series in three subgroups: never exposed, below the median, and above the median. Baggers (known length only) were also broken down in relation to calendar year and age at job entry, and years elapsed from date of job entry to date of end of follow up (or death).

Furthermore, using a job-exposure matrix made up by Pirastu and colleagues,13 we estimated the cumulative VCM exposure by summing across the calendar years of exposure the products of VCM average level in a job (ppm) by the years worked in that job. The variable was split in three classes using the tertiles (less than 392, 393–1650, more than 1651 ppm/year).

The age at end of follow up (or death) was also split in three classes in relation to the tertiles: 45–57, 58–65, 66–82 years.

Smoking habits were ascertained through the clinical records and/or the health surveillance records at the PVC plant. In current smokers and in former smokers who had stopped smoking for less than 15 years, we calculated an average weighted for periods of different consumption of cigarettes. Additionally, we coded a variable: 0 in lifelong non-smokers and in ex-smokers for 15 years or more; 1 for smokers of less than 10 cigarettes/day; 2 for smokers of 11–20 cigarettes/day; and 3 for smokers of 21 or more cigarettes/day.

Interval variables were analysed by Student’s t test and frequency variables by the χ² test. At univariate analysis, the odds ratio (OR) was obtained according to Breslow and Day,14 and the exact 95% confidence interval (CI) was estimated using the statistical package StatXact.15 When a variable was broken down into classes, the lowest class was the reference subgroup at a conventional risk of 1.0. The χ² test for linear trend (χ² linear) across ordered categories was also performed.

Average cigarette consumption, age, cumulative VCM, and working years as PVC bagger or spent in PVC compounding may have been used as independent variables in a logistic regression analysis, where the dependent variable was 1 for cases and 0 for controls. The program of stepwise multiple logistic regression analysis “BMDP-LR” was used to select the variables to be included in the final model, which was estimated by means of the exact method (conditional maximum likelihood estimate) using the statistical package LogXact.16

RESULTS

Table 1 shows some general characteristics of the 38 cases and 224 controls. Age at hire, length of time working as PVC bagger, and cigarette consumption (in smokers only) were significantly greater in the cases with respect to the controls. No difference was found in cumulative VCM exposure, years of PVC compounding, and age at the end of follow up or death.

Table 2 shows the results at univariate analysis. The prevalence of smokers was higher in cases (95%) than in controls (54%). The risk of lung cancer rapidly increases with the number of cigarettes smoked daily. Being equal to unity the conventional risk of subjects with least exposure to PVC dust, the lung cancer OR was 5.60 (95% CI 2.03 to 16.3; exact two sided p value = 0.0004) in baggers with known duration of
work, and not significantly different from 1.0 in other circumstances of PVC exposure. The lung cancer risk increases proportionately with the years spent as bagger (p < 0.0001 for trend). Irrespective of the calendar period in which subjects worked as baggers, equally high lung cancer ORs were found in the two groups (similar in terms of averages of job length and cigarettes smoked) as shown in table 2. Furthermore, OR of lung cancer increases with increasing age at onset of the job (known length). Lastly, recent rather than distant exposure as a bagger has the most profound effect on lung cancer OR. No significant trends were found across the classes of increasing years of PVC compounding, cumulative VCM exposure, or age at end of the period of observation.

Table 3 shows that smoking was not associated with the years worked as bagger. Setting at 0.05 the p value for the test “F to remove”, the analysis of logistic regression found that the variables significantly influencing the risk of lung cancer were cigarettes and years as bagger, but not years spent working in PVC compounding, VCM cumulative exposure, or age. We included cigarettes and years as bagger in a final model, accounting for the influence of age by using conditional logistic regression analysis for stratified data (five year age strata). Table 4 shows the estimates of the final model. Holding constant the influence of smoking and age, a 20% excess of lung cancer risk (OR 1.20; 95% CI 1.08 to 1.35; two tailed exact p value = 0.001) was found for each extra year of work as bagger in respect of employees never exposed to PVC, compounding workers, and baggers with unknown length of job.

| Table 2 | Cases and controls in the classes of independent variables, odds ratios (OR), 95% exact confidence intervals (CI), $\chi^2$ test for trend ($\chi^2_{\text{trend}}$), and p values for two tailed tests |
|---------|---------------------------------|-----------------|----------------|-----------------|
| Smoking habits | Cases | Controls | OR | CI | $\chi^2_{\text{trend}}$ |
| Non-smokers | 2 | 103 | Reference | | |
| Smokers, 1–10 cigarettes | 1 | 37 | 1.39 | 0.02 to 27.4 | |
| Smokers, 11–20 cigarettes | 23 | 67 | 17.7‡ | 4.10 to 157.0 | 39.87‡ |
| Smokers, ≥21 cigarettes | 12 | 17 | 36.4‡ | 6.90 to 347.0 | |
| Age at end of follow up or death | | | | | |
| 45–57 years | 11 | 75 | Reference | | |
| 58–65 years | 17 | 68 | 1.71 | 0.69 to 4.32 | 0.14 |
| 66–82 years | 10 | 81 | 0.84 | 0.30 to 2.33 | |
| VCM cumulative exposure | | | | | |
| <392 ppm years | 16 | 71 | Reference | | |
| 393–1650 ppm × years | 13 | 74 | 0.78 | 0.32 to 1.87 | 2.35 |
| ≥1651 ppm × years | 9 | 79 | 0.51 | 0.18 to 1.31 | |
| Circumstances of exposure to PVC dust | | | | | |
| None of the following | 8 | 87 | Reference | | |
| PVC compounding | 8 | 49 | 1.78 | 0.54 to 5.78 | |
| Baggers (unknown length) | 5 | 55 | 0.99 | 0.24 to 3.63 | |
| Baggers (known length) | 17 | 33 | 5.60 † | 2.03 to 16.3 | |
| Baggers: duration of job | | | | | |
| No | 30 | 175 | Reference | | |
| >8.0 years | 4 | 23 | 1.10 | 0.24 to 3.28 | 0.64 |
| >8.0 years | 4 | 26 | 0.90 | 0.21 to 2.86 | |
| Baggers: calendar year at onset of job | | | | | |
| No | 21 | 191 | Reference | | |
| Before 1967 | 10 | 19 | 4.79 † | 1.73 to 12.5 | |
| Since 1967 onwards | 7 | 14 | 4.55 † | 1.38 to 13.6 | |
| Baggers: age at onset of job | | | | | |
| No | 21 | 191 | Reference | | |
| Until 33 years | 6 | 20 | 2.73 | 0.80 to 8.07 | |
| Over 33 years | 11 | 13 | 7.70 ‡ | 2.72 to 21.1 | |
| Baggers: time elapsed from onset of job to end of follow up or death | | | | | |
| No | 21 | 191 | Reference | | |
| >20 years (distant exposure) | 12 | 29 | 3.76 * | 1.51 to 8.99 | |
| ≤20 years (recent exposure) | 5 | 4 | 11.4 * | 2.21 to 60.7 | |

*p<0.01; †p<0.001; ‡p<0.0001.

<table>
<thead>
<tr>
<th>Table 3</th>
<th>Distribution of smoking habits in the classes of years worked as baggers (known length of job)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Smoking habits</td>
<td>Length of exposure as baggers</td>
</tr>
<tr>
<td></td>
<td>No.</td>
</tr>
<tr>
<td>Non-smokers</td>
<td>91</td>
</tr>
<tr>
<td>Smokers, 1–10 cigarettes/day</td>
<td>32</td>
</tr>
<tr>
<td>Smokers, 11–20 cigarettes/day</td>
<td>69</td>
</tr>
<tr>
<td>Smokers, ≥21 cigarettes/day</td>
<td>20</td>
</tr>
</tbody>
</table>

$\chi^2=8.638$, p=0.1950 (6 degrees of freedom).

| Table 4 | Lung cancer risk in relation to cigarette consumption and years of work as baggers (subjects with known duration of work) |
|---------|---------------------------------|-----------------|
| Terms | OR | CI | p value |
| Average number of cigarettes* | 1.1077 | 1.0645 to 1.1583 | 2.22E-08 |
| Baggers (years)† | 1.2003 | 1.0772 to 1.3469 | 0.0010 |

Estimated using conditional logistic regression analysis for stratified data (strata: five year age): model terms (TERMS), odds ratio (OR), exact 95% confidence interval (CI), exact error probability (p) for two tailed test.

*OR = 1 among non-smokers.
†OR = 1 among subjects: never exposed to PVC dusts; exposed to PVC but not baggers; and baggers with unknown duration of work.
and the present study.

At the beginning of the trial, the company granted compensa-
tion to all the diseased subjects in the cohort. It is therefore im-
portant to consider whether our method for selecting controls
may have introduced a bias. If disease occurred in controls
because exposure was higher than, similar to, or lower than
that in the whole cohort, the lung cancer risk would have been
underestimated. In the same European cohort, a lung cancer risk
attributed to their exposure if PVC dust concentration was
above the threshold limit value (TLV, equal to 10 mg/m$^3$).
Exposure to PVC dust was measured at our plant (see below). Job is not an accurate sur-
rogate for occupational exposure; therefore, Jones and
colleagues’ results$^3$ could not be used to assess any level of
exposure to PVC dust from lung cancer risk.

PVC bagging was used as surrogate of exposure to PVC dust
in the European cohort of vinyl chloride workers. Lung cancer
risk in PVC exposed workers was probably underestimated. In the same European cohort, a
trend with cumulative VCM exposure was found for lung can-
cer risk in subjects who had only worked as packers and bag-
gers. Since in these workers cumulative VCM exposure could
be proportional to their length of PVC exposure, our interpret-
ation is that the risk factor involved is PVC rather than VCM
exposure.

Table 5 shows that on using Dunn’s method,$^{16}$ there was an
agreement of 54% between the lung cancer diagnoses based
on either death certificate (Comba P and Pirastu R, personal
communication on the extension of follow up to July 1999) or
histology (present study).

Table 6 shows a poor agreement (Cohen’s kappa = 0.348) in
the definition of PVC bagger (known exposure only) between
the study of Comba and Pirastu (personal communication) and the present study.

DISCUSSION

At the beginning of the trial, the company granted compensa-
tion to all the diseased subjects in the cohort. It is therefore im-
portant to consider whether our method for selecting controls
may have introduced a bias. If disease occurred in controls
because exposure was higher than, similar to, or lower than
that in the whole cohort, the lung cancer risk would have been
underestimated, valid, or overestimated, respectively. The first
two hypotheses seem more likely than the last. Therefore, ours
is a case-control study nested in a cohort, where the particular
selection of the controls may have underestimated the risk of
lung cancer.

Baggers with unknown length of work are 5/38 cases (13%)
and 55/224 controls (25%), and the difference between the
two proportions is not significant. If these subjects carry prob-
lems of misclassification, the misclassification is non-
differential and the direction of the bias is towards the null
hypothesis, leading the OR to near unity (table 2). Because of
possible information bias in baggers with unknown length of
duty, the conclusive risk of lung cancer is the one estimated
in PVC baggers with known length of exposure.

Smoking is a cause of lung cancer, but in our study it was not
associated with the years of known duration of PVC bag-
ing (table 3), even though there was a tendency for cigarette
consumption to increase with the increasing number of years
worked as PVC bagger.

In the reference group at conventional risk of 1.0, we
grouped workers never exposed to PVC dust together with:
workers engaged in PVC compounding; PVC baggers with
unknown length of job; autoclave workers (exposed to PVC
dust during the removal of residual material from the inside
of large reactor vessels); and driers (exposed during the mainte-
nance of the drying room in case of malfunction). Inclusion of
such workers at lower PVC exposure may have underesti-
ated the risk of lung cancer.

Of the five studies in which the lung cancer risk was
analysed with respect to both PVC and VCM exposure, three
supported our findings,$^{13,19}$ although in the third study the
lung cancer risk was biased by misclassification of both
disease (table 5) and exposure (table 6).

The conflicting information reported in the remaining two
studies may be mistaken or misinterpreted. Wu and
colleagues’ report discrepant results (the lung cancer cases
exposed to VCM are 80 in table 4 and 96 in table 6) and illogi-
cal facts (since incomplete polymerisation reactions leave
amounts of monomer unreacted in the PVC dust, more work-
ers with lung cancer would have VCM exposure than PVC
exposure, not less, as shown in table 6). Jones and colleagues$^4$
report a low risk of lung cancer, which may be explained by
the low level of PVC dust in baggers-driers ranging from 0.38
to 2.88 mg/m$^3$, an order of magnitude lower than that
measured at our plant (see below). Job is not an accurate sur-
rogate for occupational exposure; therefore, Jones and
colleagues’ results$^3$ could not be used to assess any level of
exposure to PVC dust from lung cancer risk.

Table 5

<table>
<thead>
<tr>
<th>Lung cancer cases defined by death certificate in Comba and Pirastu’s study* and by histology in the present study</th>
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<tbody>
<tr>
<td>Present study</td>
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<tr>
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<tr>
<td></td>
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<tr>
<td>Yes</td>
</tr>
<tr>
<td>No</td>
</tr>
</tbody>
</table>

Agreement measure (Dunn, 1992):
$27/(27+12+11) = 54%$.

*Personal communication: extension of cohort follow up to 1 July 1999.

Table 6

<table>
<thead>
<tr>
<th>Workers classified as baggers (known length of exposure) in the present and in Comba and Pirastu’s study*</th>
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</thead>
<tbody>
<tr>
<td>Present study</td>
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<tr>
<td>---------------</td>
</tr>
<tr>
<td>Others</td>
</tr>
<tr>
<td>Baggers</td>
</tr>
<tr>
<td>Total</td>
</tr>
</tbody>
</table>

*Personal communication: extension of cohort follow up to 1 July 1999.
reported by Casula et al in a similar Italian facility.14 In the PVC baggers, air samples were collected by means of personal samples during three 8-hour work shifts. The mean values (range) of PVC concentrations were 7.0 mg/m³ (0.67–39.3 mg/m³) in the suspension and 5.19 mg/m³ (0.28–23.4 mg/m³) in the emulsion polymerisation departments. Given that the respirable dust was more than 90% of the dust’s sample weight, these values were about twice the TLV (3 mg/m³).

The calendar time of major changes in the process, or of major hygienic improvements such as the installation of exhaust ventilation systems, can be used as proxies of past exposure. At our plant, exhaust ventilation systems were first installed in a sack department in 1982, and the loading of PVC dust in containers, instead of manual bagging, was introduced in 1985. Thus, reasonably, the high levels measured prior to 1979 remained elevated until the early 1980s, when most of the lung cancer cases were no longer working as PVC baggers. The extremely high dustiness of the job was admitted by the management: it was only mandatory for PVC baggers to take a shower (and they had half an hour paid to do so) at the end of the workshift.

Although all these sources of information were consistent, the available measures were too few and sparse. We therefore used years of PVC bagger duration as surrogate for cumulative exposure in analysing the exposure-effect relation between PVC dust and lung cancer risk.

Inhaled PVC dust particles smaller than 5 μm may remain in the pulmonary interstitium for years, gradually releasing the residual VCM which, according to Waxweiler and colleagues, may account for the neoplastic transformation of the epithelial cell. However, cytotoxic P450-2E1, required to activate the indirect acting carcinogen VCM, is present in human healthy pulmonary tissues in only a proportion of the studied individuals.19–23 If the activating enzyme is inducible in human lung—with smoking as in mouse lung24 and with chronic ethanol consumption as in rat lung25—the interindividual variability would be accrued, thus explaining the lack of relation between lung cancer risk and cumulative VCM exposure (table 2).

Lung fibrosis was histologically ascertained in cases of PVC pneumoenosis.20–22 Lung changes consistent with interstitial fibrosis were also reported by Cordasco and colleagues24 in a 41 year old subject having extensive daily use of VCM spray paint for 14 years in the dental mould industry, and by Prodan and colleagues25 in experimental animals with chronic exposure to VCM. Therefore, PVC and/or VCM exposure can induce lung cancer through pulmonary fibrosis, like that which occurs in pulmonary idiopathic fibrosis,26 cryptogenic fibrosing alveolitis,27 fibrosis connected to collagen diseases,28 asbestosis,29 and silicosis.30

Production of a polypeptide growth factor for alveolar type II, which is probably a high molecular weight precursor of transforming growth factor α (considered to be a strong stimulant for epithelial cell proliferation),31 has been observed in rabbit alveolar macrophages exposed in vitro to PVC particles.32 PVC dust, remaining in the pulmonary interstitium for years, may act as a promoter, inducing clonal expansion of mutated cells; under repeated proliferative stimuli the number of mutations increases more and more, leading the cell to malignant transformation. The role of PVC dust as “promoting” carcinogen operating in the last phases of lung carcinogenesis concurs with epidemiological data in PVC baggers. In our baggers, recent rather than distant exposure to PVC dust had the most profound effects on lung cancer risk, which, moreover, increased with increasing age at first exposure (table 2). In the study by Comba and Pirastu,33 lung cancer risk in baggers decreased with increasing latency (observed/expected equal to 4.2 3 and 64.8, SMR equal to 1.75 and 1.25, when latency was lower or, respectively, higher than 20 years). Lastly, Berrino,34 reanalysing the data from the European cohort of vinyl chloride workers, found that lung cancer 5SMR reduced from 1.74 to 1.52 by subtracting a 15 year lag from work histories in subjects with cumulative VCM exposure higher than 100 ppm/year who had only worked as packers and baggers.

No cancer excess was found in long term inhalation studies,35–40 nor could it be expected given that the level of exposure to PVC dust was similar (concentrations ranged from 10 to 20 mg/m³) with respect to that in PVC baggers. By contrast, rodents are generally exposed to levels of carcinogen orders of magnitude higher than that in workplaces. Analogous to what has been reported for other non-genotoxic non-soluble dusts with low toxicity (carbon black, toner, talc, titanium dioxide), long term inhalation of high concentrations of PVC dust could act as a carcinogenic effect in experimental animals, since the events triggering the carcinogenic transformation (persistent alveolar inflammation, alveolar macrophage activation, release of chitokines, chemokines, and growth factors) were also reported for PVC dust.35–36

Therefore, whenever a case of PVC pneumoenosis was reported,37–41 or airborne levels of PVC dust were high,32 a correlative increase in lung cancer risk would be expected in PVC baggers. Since classic tumour promoters have a threshold below which no response occurs, no lung cancer risk should be found in industries or jobs involving low exposure to PVC dust. Further studies (or better, a cooperative larger study) are advised in order to confirm the present findings. In designing new epidemiological studies, our experience emphasises the need to reduce misclassification of exposure and disease. New mechanistic studies are also warranted.

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1.2003; 95% CI 1.0772 to 1.3469; p = 0.0010), after controlling the influence of age and smoking habits.

The excess lung cancer risk may be attributed to exposure since PVC dust concentration was high and particle size was compatible with the effect in study.

Lung cancer risk is generally low in cohort studies due to a dilution effect from poor characterisation of the relevant exposure (VCM instead of PVC).

Main messages

• By using a nested case-control approach we found in the VCM/PVC industry that the lung cancer risk increases by 20% for each extra year of work as a PVC bagger (OR 1.2003; 95% CI 1.0772 to 1.3469; p = 0.0010), after controlling the influence of age and smoking habits.

Policy implications

• Our findings indicate that working longer than 3.5 years as a PVC bagger increases above twofold the lung cancer risk.

• Although PVC dust is currently classified in group 3 by IARC and as a nuisance dust by ACGIH, and although new experimental and epidemiological studies are needed, our findings and sparse experimental and epidemiological evidence points out that PVC may have a carcinogenic effect.

• These conclusions should lead policy makers to apply the “precautionary principle” to the control of PVC dust.
REFERENCES


34. Finkelstein JN. Physiological and toxicologic response of alveolar type II cells. Toxicology 1990;60:41–52.


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